AMENDMENT

In the Specification:

Please replace the entire specification from the parent application, other than the claims, with the enclosed substitute specification.

In the Claims:

The accompanying paper requests cancellation of all pending claims except claim 1, without prejudice or disclaimer.

Please further cancel claim 1, after according a filing date to this application.

Please add new claims 11-53, as follows:

11. A phosphoinositide analogue based on di-*O*-fattyacyl (or alkyl)-*sn*-glycero-3'-phospho-*myo*-inositol or di-*O*-fattyacyl (or alkyl)-*sn*-glycero-3'-phospho-*scyllo*-inositol having at least one additional hydroxyl group derivatized as a phosphate, wherein said phosphoinositide analogue incorporates one or more of the following modifying structural features:

(a) the 2-OH is rendered non-nucleophilic by derivatization or replacement; or

(b) a reporter group or conjugand is incorporated in the fatty acyl or inositol residue;

wherein the core structure and absolute stereochemistry of the unmodified di-*O*-fattyacyl (or alkyl)-*sn*-glycero-3'-phospho-*myo*-inositol phosphate or di-*O*-fattyacyl (or alkyl)-*sn*-glycero-3'-phospho-*scyllo*-inositol phosphate is maintained in said phosphoinositide analogue.

12. The phosphoinositide analogue of claim 11, wherein said phosphoinositide analogue is a phosphoinositide-(mono-phosphate) analogue.

13. The phosphoinositide analogue of claim 11, wherein said phosphoinositide analogue is a phosphoinositide-(di-phosphate) analogue.

14. The phosphoinositide analogue of claim 13, wherein said phosphoinositide analogue is a PtdIns(4,5)P_2 analogue.

15. The phosphoinositide analogue of claim 11, wherein said phosphoinositide analogue is a phosphoinositide-(poly-phosphate) analogue.

16. The phosphoinositide analogue of claim 11, wherein the 2-OH is rendered non-nucleophilic by derivatization or replacement.

17. The phosphoinositide analogue of claim 16, wherein the 2-OH is rendered non-nucleophilic by derivatization.

18. The phosphoinositide analogue of claim 17, wherein the 2-OH is rendered non-nucleophilic by derivatization to form a 2-OCOR or 2-OR phosphoinositide analogue, wherein R is alkyl, substituted alkyl or alkenyl.

19. The phosphoinositide analogue of claim 18, wherein the 2-OH is rendered non-nucleophilic by derivatization to form 2-*O*Ac.

10. 20. The phosphoinositide analogue of claim 8, 18, wherein the 2-OH is rendered non-nucleophilic by derivatization to form a 2-OCOR or 2-OR phosphoinositide analogue, wherein R is CH_3.

11. 21. The phosphoinositide analogue of claim 8, 18, wherein the 2-OH is rendered non-nucleophilic by derivatization to form a 2-OCOR or 2-OR phosphoinositide analogue, wherein R is ω-amino-alkyl.

12. 22. The phosphoinositide analogue of claim 8, 18, wherein the 2-OH is rendered non-nucleophilic by derivatization to form a 2-OCOR or 2-OR phosphoinositide analogue, wherein R is N-substituted-ω-amino-alkyl.

13. 23. The phosphoinositide analogue of claim 8, 18, wherein the 2-OH is rendered non-nucleophilic by derivatization to form a 2-OCOR or 2-OR phosphoinositide analogue, wherein R is N,N-disubstituted-ω-amino-alkyl.

14. 24. The phosphoinositide analogue of claim 6, 16, wherein the 2-OH is rendered non-nucleophilic by replacement.

15. 25. The phosphoinositide analogue of claim 14, 24, wherein the 2-OH is rendered non-nucleophilic by replacement to form the 2-deoxyhalo or 2-dideoxyhalo phosphoinositide analogue.

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26. The phosphoinositide analogue of claim 25, wherein the 2-OH is rendered non-nucleophilic by replacement to form the 2-deoxyfluoro phosphoinositide analogue.

27. The phosphoinositide analogue of claim 11, wherein a reporter group or conjugand is incorporated in the fatty acyl or inositol residue.

28. The phosphoinositide analogue of claim 27, wherein a reporter group is incorporated.

29. The phosphoinositide analogue of claim 28, wherein the reporter group is a photoaffinity reporter group.

30. The phosphoinositide analogue of claim 28, wherein the reporter group is a fluorescent reporter group.

31. The phosphoinositide analogue of claim 28, wherein the reporter group is a spin probe reporter group.

32. The phosphoinositide analogue of claim 28, wherein the reporter group is a radioactive label reporter group.

33. The phosphoinositide analogue of claim 28, wherein the reporter group is a stable isotope label reporter group.

24
34. The phosphoinositide analogue of claim 27, wherein a conjugand is incorporated.

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35. The phosphoinositide analogue of claim 24, wherein the conjugand is alkyl-C=O, ω-NH_2-alkyl-C=O, ω-NH_2-alkyl, ω-thio-(alkyl-C=O) or ω-thio-alkyl.

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36. The phosphoinositide analogue of claim 24, wherein the conjugand is suitable for linking the phosphoinositide analogue to a polymer.

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37. The phosphoinositide analogue of claim 24, wherein the conjugand is suitable for linking the phosphoinositide analogue to a chromatographic matrix.

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38. The phosphoinositide analogue of claim 24, wherein the conjugand is suitable for linking the phosphoinositide analogue to a gold surface.

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39. The phosphoinositide analogue of claim 24, wherein the conjugand is suitable for linking the phosphoinositide analogue to a reporter group.

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40. The phosphoinositide analogue of claim 1, wherein one or both glycerol esters are replaced by ether bonds.

31
41. A selectively *O*-protected phosphoinositide analogue obtained as a phosphodiester intermediate formed by the reaction of a selectively protected *myo*-inositol phosphate or *scyllo*-

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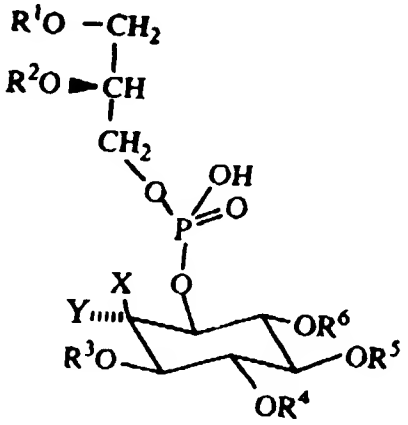
inositol phosphate and an *sn*-3-phosphatidic acid or glycero-ether analogue, wherein the said *O*-protected phosphoinositide analogue has the structure:



wherein at least one of R^3, R^4, R^5, R^6 is P(=O)(O-protecting group)$_2$,

and wherein:

(a) X = F, Cl, Br, OC(=O)R, OR, or P(=O)(O-protecting group)$_2$, and Y = H; or

X = Y = H; or

(b) X = H, and Y = F, Cl, Br, OC(=O)R, OR, or P(=O)(O-protecting group)$_2$; or

(c) X = Y = F or (=O);

where R = alkyl, especially methyl or ethyl, alkenyl, alkynyl, ω-aminoalkyl, N-substituted-ω-aminoalkyl or N,N-disubstituted-ω-aminoalkyl;

and wherein

(d) R^1 = RC(=O) or R, R^2 = R'C(=O) or R'

where R, R' = alkyl or alkenyl;

and wherein:

(e) R^3 = H, or P(=O)(O-protecting group)$_2$,

(f) R^4 = H, or P(=O)(O-protecting group)$_2$,

(g) R^5 = H, or P(=O)(O-protecting group)$_2$,

(h) R^6 = H, P(=O)(O-protecting group)$_2$, ω-aminoalkyl, ω-aminoalkenyl, ω-sulfhydrylalkyl, ω-carboxyalkyl, ω-(4-azidosalicylamido)-alkyl, alkyl-aminofluorophor, alkyl-amidofluorophor, or alkyl-fluorophor.

42. The phosphoinositide analogue of claim 11, wherein:

(a) the 2-OH is rendered non-nucleophilic by derivatization or replacement; and

(b) a reporter group or conjugand is incorporated in the fatty acyl or inositol residue;

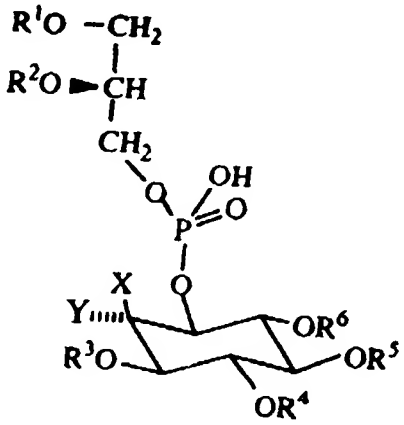
wherein the core structure and absolute stereochemistry of the unmodified di-*O*-fattyacyl (or alkyl)-*sn*-glycero-3'-phospho-*myo*-inositol phosphate or di-*O*-fattyacyl (or alkyl)-*sn*-glycero-3'-phospho-*scyllo*-inositol phosphate is maintained in said phosphoinositide analogue.

43. A phosphoinositide analogue based on di-*O*-fattyacyl (or alkyl)-*sn*-glycero-3'-phospho-*myo*-inositol or di-*O*-fattyacyl (or alkyl)-*sn*-glycero-3'-phospho-*scyllo*-inositol having at least one additional hydroxyl group derivatized as a phosphate, wherein the 2-OH is rendered non-nucleophilic by derivatization or replacement and wherein the core structure and absolute stereochemistry of the unmodified di-*O*-fattyacyl (or alkyl)-*sn*-glycero-3'-phospho-*myo*-inositol phosphate or di-*O*-fattyacyl (or alkyl)-*sn*-glycero-3'-phospho-*scyllo*-inositol phosphate is maintained in said phosphoinositide analogue.

44. The phosphoinositide analogue of claim 11, wherein said phosphoinositide analogue is based on di-*O*-fattyacyl (or alkyl)-*sn*-glycero-3'-phospho-*myo*-inositol phosphate.

45. The phosphoinositide analogue of claim 11, wherein said phosphoinositide analogue is based on di-*O*-fattyacyl (or alkyl)-*sn*-glycero-3'-phospho-*scyllo*-inositol phosphate.

46. A selectively *O*-protected phosphoinositide analogue obtained as a phosphodiester intermediate formed by the reaction of a selectively protected *myo*-inositol phosphate or *scyllo*-inositol phosphate and an *sn*-3-phosphatidic acid or glycero ether analogue, wherein the said *O*-protected phosphoinositide analogue has the structure:



wherein at least one of R^3, R^4, R^5, R^6 is P(=O)(O-protecting group)$_2$,

and wherein

(a) X = OH, and Y = H; or X = H, and Y = OH;

and wherein

(b) R^1 = RC(=O) or R, R^2 = R'C(=O) or R'

where R = alkyl, alkenyl, alkynyl, R' = ω-aminoalkyl, ω-(substitutedamino)-alkyl, ω-aminoalkenyl, ω-sulfhydrylalkyl, ω-carboxyalkyl, ω-(4-azidosalicylamido)-alkyl, ω-(substitutedamido)-alkyl, alkyl-aminofluorophor, alkyl-amidofluorophor, alkyl-fluorophor, hydroxylalkyl, or ketoalkyl; or where R'= alkyl, alkenyl, alkynyl, R = ω-aminoalkyl, ω-(substitutedamino)-alkyl, ω-aminoalkenyl, ω-sulfhydrylalkyl, ω-carboxyalkyl, ω-(4-azidosalicylamido)-alkyl, ω-(substitutedamido)-alkyl, alkyl-aminofluorophor, alkyl-amidofluorophor, alkyl-fluorophor, hydroxylalkyl, or ketoalkyl; or where R = R', except when R = R' = alkyl;

and wherein

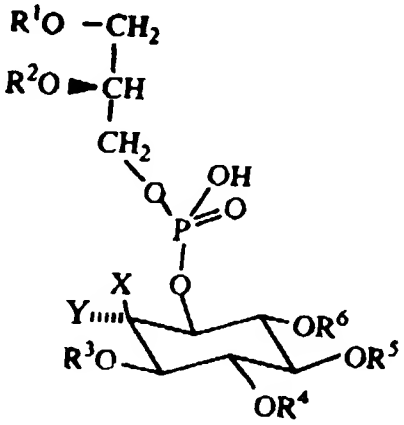
(c) R^3 = H, or P(=O)(O-protecting group)$_2$,

(d) R^4 = H, or P(=O)(O-protecting group)$_2$,

(e) R^5 = H, or P(=O)(O-protecting group)$_2$,

(f) R^6 = H, P(=O)(O-protecting group)$_2$, ω-aminoalkyl, ω-aminoalkenyl, ω-sulfhydrylalkyl, ω-carboxyalkyl, ω-(4-azidosalicylamido)-alkyl, alkyl-aminofluorophor, alkyl-amidofluorophor, or alkyl-fluorophor.

47. A selectively *O*-protected phosphoinositide analogue obtained as a phosphodiester intermediate formed by the reaction of a selectively protected *myo*-inositol phosphate or *scyllo*-inositol phosphate and an *sn*-3-phosphatidic acid or glycero ether analogue, wherein the said *O*-protected phosphoinositide analogue has the structure:



wherein at least one of R^3, R^4, R^5, R^6 is $P(=O)(O\text{-protecting group})_2$,

and wherein

(a) X = F, Cl, Br, OC(=O)R, OR, or $P(=O)(O\text{-protecting group})_2$, and Y = H; or

X = Y = H; or

(b) X = H, and Y = F, Cl, Br, OC(=O)R, OR, or $P(=O)(O\text{-protecting group})_2$, or

(c) X = Y = F or (=O);

where R = alkyl, especially methyl or ethyl, alkenyl, alkynyl, ω-aminoalkyl, N-substituted-ω-aminoalkyl or N,N-disubstituted-ω-aminoalkyl;

and wherein

(d) $R^1 = RC(=O)$ or R, $R^2 = R'C(=O)$ or R'

where R = alkyl, alkenyl, alkynyl, R' = ω-aminoalkyl, ω-(substitutedamino)-alkyl, ω-aminoalkenyl, ω-sulfhydrylalkyl, ω-carboxyalkyl, ω-(4-azidosalicylamido)-alkyl, ω-(substitutedamido)-alkyl, alkyl-aminofluorophor, alkyl-amidofluorophor,

alkyl-fluorophor, hydroxylalkyl, or ketoalkyl; or where R' = alkyl, alkenyl, alkynyl, R = ω-aminoalkyl, ω-(substitutedamino)-alkyl, ω-aminoalkenyl, ω-sulfhydrylalkyl, ω-carboxyalkyl, ω-(4-azidosalicylamido)-alkyl, ω-(substitutedamido)-alkyl, alkyl-aminofluorophor, alkyl-amidofluorophor, alkyl-fluorophor, hydroxylalkyl, or ketoalkyl; or where R = R';

and wherein

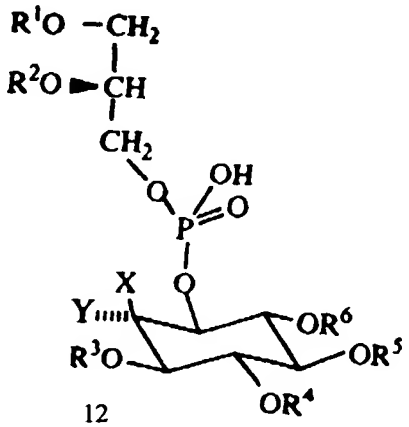
(e) R^3 = H, or P(=O)(O-protecting group)$_2$,

(f) R^4 = H, or P(=O)(O-protecting group)$_2$,

(g) R^5 = H, or P(=O)(O-protecting group)$_2$,

(h) R^6 = H, P(=O)(O-protecting group)$_2$, ω-aminoalkyl, ω-aminoalkenyl, ω-sulfhydrylalkyl, ω-carboxyalkyl, ω-(4-azidosalicylamido)-alkyl, alkyl-aminofluorophor, alkyl-amidofluorophor, or alkyl-fluorophor.

48. A phosphoinositide analogue based on phosphatidylinositolphosphate, wherein the 2-OH is rendered non-nucleophilic by derivatization or replacement or wherein a reporter group or conjugand is incorporated in the fatty acyl or inositol residue; wherein the core structure and absolute stereochemistry of the unmodified phosphatidylinositolphosphate is maintained in said phosphoinositide analogue; and wherein said phosphoinositide analogue has the structure:



wherein at least one of R^3, R^4, R^5, R^6 is $P(=O)(OH)_2$,

and wherein

(a) X = F, Cl, Br, $OC(=O)R$, OR, or $OP(=O)(OH)_2$, and Y = H; or

X = Y = H; or

(b) X = H, and Y = F, Cl, Br, $OC(=O)R$, OR, or $OP(=O)(OH)_2$; or

(c) X = Y = F or (=O);

where R = alkyl, especially methyl or ethyl, alkenyl, alkynyl, ω-aminoalkyl, N-substituted-ω-aminoalkyl or N,N-disubstituted-ω-aminoalkyl;

and wherein

(d) $R^1 = RC(=O)$ or R, $R^2 = R'C(=O)$ or R'

where R, R' = alkyl or alkenyl;

and wherein

(e) R^3 = H, or $P(=O)(OH)_2$

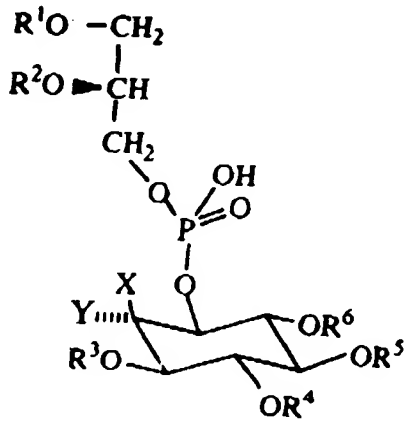
(f) R^4 = H, or $P(=O)(OH)_2$

(g) R^5 = H, or $P(=O)(OH)_2$

(h) R^6 = H, $P(=O)(OH)_2$, ω-aminoalkyl, ω-aminoalkenyl, ω-sulfhydrylalkyl, ω-carboxyalkyl, ω-(4-azidosalicylamido)-alkyl, alkyl-aminofluorophor, alkyl-amidofluorophor, or alkyl-fluorophor.

39.

49. A phosphoinositide analogue based on phosphatidylinositolphosphate, wherein the 2-OH is rendered non-nucleophilic by derivatization or replacement or wherein a reporter group or conjugand is incorporated in the fatty acyl or inositol residue; wherein the core structure and absolute stereochemistry of the unmodified phosphatidylinositolphosphate is maintained in said phosphoinositide analogue; and wherein said phosphoinositide analogue has the structure:



wherein at least one of R^3, R^4, R^5, R^6 is $P(=O)(OH)_2$,

and wherein

(a) X = OH, and Y = H; or X = H, and Y = OH;

and wherein

(b) R^1 = RC(=O) or R, R^2 = R'C(=O) or R'

where R = alkyl, alkenyl, alkynyl, R' = ω-aminoalkyl, ω-(substitutedamino)-alkyl, ω-aminoalkenyl, ω-sulfhydrylalkyl, ω-carboxyalkyl, ω-(4-azidosalicylamido)-alkyl, ω-(substitutedamido)-alkyl, alkyl-aminofluorophor, alkyl-amidofluorophor, alkyl-fluorophor, hydroxylalkyl, or ketoalkyl; or where R' = alkyl, alkenyl, alkynyl, R = ω-aminoalkyl, ω-(substitutedamino)-alkyl, ω-aminoalkenyl,

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ω-sulfhydrylalkyl, ω-carboxyalkyl, ω-(4-azidosalicylamido)-alkyl, ω-(substitutedamido)-alkyl, alkyl-aminofluorophor, alkyl-amidofluorophor, alkyl-fluorophor, hydroxylalkyl, or ketoalkyl; or where R = R', except when R = R' = alkyl;

and wherein

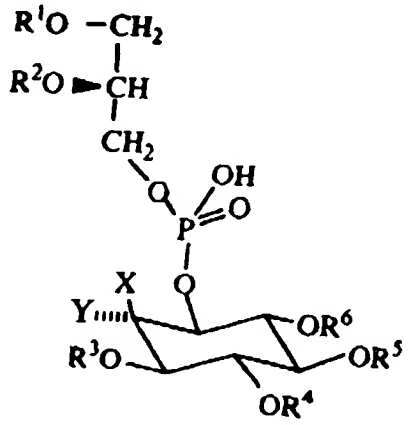
(c) R^3 = H, or $P(=O)(OH)_2$

(d) R^4 = H, or $P(=O)(OH)_2$

(e) R^5 = H, or $P(=O)(OH)_2$

(f) R^6 = H, $P(=O)(OH)_2$, ω-aminoalkyl, ω-aminoalkenyl, ω-sulfhydrylalkyl, ω-carboxyalkyl, ω-(4-azidosalicylamido)-alkyl, alkyl-aminofluorophor, alkyl-amidofluorophor, or alkyl-fluorophor.

50. A phosphoinositide analogue based on phosphatidylinositolphosphate, wherein the 2-OH is rendered non-nucleophilic by derivatization or replacement and a reporter group or conjugand is incorporated in the fatty acyl or inositol residue; wherein the core structure and absolute stereochemistry of the unmodified phosphatidylinositolphosphate is maintained in said phosphoinositide analogue; and wherein said phosphoinositide analogue has the structure:



wherein at least one of R^3, R^4, R^5, R^6 is $P(=O)(OH)_2$,

and wherein

(a) X = F, Cl, Br, OC(=O)R, OR, or $OP(=O)(OH)_2$, and Y = H; or

X = Y = H; or

(b) X = H, and Y = F, Cl, Br, OC(=O)R, OR, or $OP(=O)(OH)_2$; or

(c) X = Y = F or (=O);

where R = alkyl, especially methyl or ethyl, alkenyl, alkynyl, ω-aminoalkyl, N-substituted-ω-aminoalkyl or N,N-disubstituted-ω-aminoalkyl;

and wherein

(d) R^1 = RC(=O) or R, R^2 = R'C(=O) or R'

where R = alkyl, alkenyl, alkynyl, R' = ω-aminoalkyl, ω-(substitutedamino)-alkyl, ω-aminoalkenyl, ω-sulfhydrylalkyl, ω-carboxyalkyl, ω-(4-azidosalicylamido)-alkyl, ω-(substitutedamido)-alkyl, alkyl-aminofluorophor, alkyl-amidofluorophor, alkyl-fluorophor, hydroxylalkyl, or ketoalkyl; or where R' = alkyl, alkenyl, alkynyl, R = ω-aminoalkyl, ω-(substitutedamino)-alkyl, ω-aminoalkenyl, ω-sulfhydrylalkyl, ω-carboxyalkyl, ω-(4-azidosalicylamido)-alkyl, ω-(substitutedamido)-alkyl, alkyl-aminofluorophor, alkyl-amidofluorophor, alkyl-fluorophor, hydroxylalkyl, or ketoalkyl; or where R = R';

and wherein

(e) R^3 = H, or $P(=O)(OH)_2$

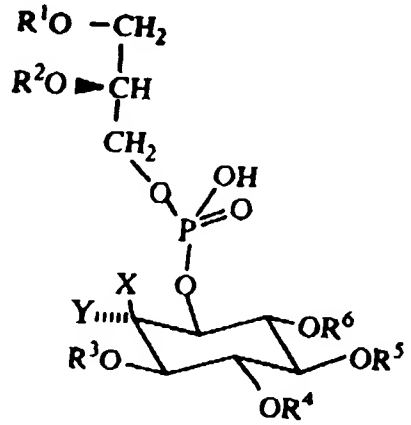
(f) R^4 = H, or $P(=O)(OH)_2$

(g) R^5 = H, or $P(=O)(OH)_2$

(h) R^6 = H, $P(=O)(OH)_2$, ω-aminoalkyl, ω-aminoalkenyl, ω-sulfhydrylalkyl, ω-carboxyalkyl, ω-(4-azidosalicylamido)-alkyl, alkyl-aminofluorophor, alkyl-amidofluorophor, or alkyl-fluorophor.

51. Matched pairs of the 2-modified phosphatidylinositol-phosphates of claim 48 and the corresponding phosphatidylinositol-phosphate structure lacking the 2-modification, wherein X=OH and Y=H, or X=H and Y=OH.

52. The phosphoinositide analogue of claim 11, wherein said phosphoinositide analogue has the structure:



wherein at least one of R^3, R^4, R^5, R^6 is $P(=O)(OH)_2$,

and wherein

(a) X = OH, and Y = H; or X = H, and Y = OH

and wherein

(b) R^1 = RC(=O) or R, R^2 = R'C(=O) or R'

where R = alkyl, alkenyl, alkynyl, R' = ω-aminoalkyl, ω-(substitutedamino)-alkyl, ω-aminoalkenyl, ω-sulfhydrylalkyl, ω-carboxyalkyl, ω-(4-azidosalicylamido)-alkyl, ω-(substitutedamido)-alkyl, alkyl-aminofluorophor, alkyl-amidofluorophor, [alkyl-fluorophor], hydroxylalkyl, or ketoalkyl; or where R' = alkyl, alkenyl, alkynyl, R = ω-aminoalkyl, ω-(substitutedamino)-alkyl, ω-aminoalkenyl, ω-sulfhydrylalkyl, ω-carboxyalkyl, ω-(4-azidosalicylamido)-alkyl, ω-(substitutedamido)-alkyl, alkyl-aminofluorophor, alkyl-amidofluorophor, hydroxylalkyl, or ketoalkyl;

and wherein

(c) R^3 = H, or $P(=O)(OH)_2$

(d) R^4 = H, or $P(=O)(OH)_2$

(e) R^5 = H, or $P(=O)(OH)_2$

(f) R^6 = H, $P(=O)(OH)_2$, ω-aminoalkyl, ω-aminoalkenyl, ω-sulfhydrylalkyl, ω-carboxyalkyl, ω-(4-azidosalicylamido)-alkyl, alkyl-aminofluorophor, alkyl-amidofluorophor, or alkyl-fluorophor.

53. A phosphoinositide analogue based on di-*O*-fattyacyl (or alkyl)-*sn*-glycero-3'-phospho-*myo*-inositol or di-*O*-fattyacyl (or alkyl)-*sn*-glycero-3'-phospho-*scyllo*-inositol having at least one additional hydroxyl group derivatized as a phosphate, wherein said phosphoinositide analogue incorporates one or more of the following modifying structural features:

(a) the 2-OH is rendered non-nucleophilic by derivatization or replacement; or